UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/670,399	09/27/2000	Masao Washizu	001268	7255

23850 7590 03/01/2006

ARMSTRONG, KRATZ, QUINTOS, HANSON & BROOKS, LLP
1725 K STREET, NW
SUITE 1000
WASHINGTON, DC 20006

EXAMINER	
BROWN, JENNINE M	

ART UNIT	PAPER NUMBER
1755	

DATE MAILED: 03/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/670,399	WASHIZU ET AL.	
	Examiner	Art Unit	
	Jennine M. Brown	1755	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Specification

The objections set forth in the previous office action have been withdrawn in view of applicant's arguments.

The phrase "or the like" render the specification indefinite because the specification includes elements not actually disclosed (those encompassed by "or the like"), thereby rendering the scope unascertainable. See MPEP § 2173.05(d).

Claim Objections

The objections set forth in the previous office action have been withdrawn in view of applicant's arguments.

The previous objection to Claim 14 has been obviated by applicant's amendment therefore this objection has been withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The disclosure and claims both have terms and/or phrases in quotation marks. Applicant stated this enclosure in quotation marks is used to grammatically designate the subject matter as special but that the meaning would be understood by one of

ordinary skill in the art. Nonetheless, the special designation of the terms through the use of quotation marks does not provide a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains. The special way that applicant means to designate these terms is unclear in that their ordinary meaning would now not be applicable. That is, how is "specific molecule" different from specific molecule?

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for conductive material made of gold and aluminum, does not reasonably provide enablement for or the like. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. What other conductive materials would be included or excluded by or the like?

Claims 1-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the following molecules: nucleotide chains, oligonucleotide chains, polynucleotide chains, chromosomes, peptide chains, C-peptide, angiotensin 1, proteins, immunoglobulin A (IgA), immunoglobulin E (IgE), immunoglobulin G (IgG), ß2-microglobulin, albumin, and ferritin, enzyme proteins, amylase, alkaline phosphatase, and y-glutamyltransferase, antiviral antibodies, viruses, Rubella virus, Herpes virus, Hepatitis virus, ATL virus, and AIDS virus, antigens, antibodies, lipids, lipoproteins, proteases, trypsin, plasmin, serine proteases, G-

fetoprotein, CA19-9, prostate-specific antigen, carcinoembryonic antigen, lectins, concanavalin A, Lens culinaris lectin, Phaseolus vulgaris lectin, Dutura stramonium lectin, wheat germ lectin, isozymes, hormones, alkaline phosphatase, acid phosphatase, y-glutamyltransferase (y-GTP), lipase, creatine kinase (CK), lactate dehydrogenase (LDH), glutamic-oxaloacetic transaminase (GOT), glutamic-pyruvic transaminase (GPT), renin, protein kinases, tyrosine kinases, steroid hormones, human chorionic gonadotropin (hCG), prolactin, thyroid-stimulating hormone (TSH), luteinizing hormone (LH), prostate-specific antigen (PSA), α2-macroglobulin, carcinoembryonic antigen (CEA), G-fetoprotein, does not reasonably provide enablement for and the like. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. No two methods used would be exactly the same for a separation because the molecules themselves have different properties which would affect a separation, how can one method cover such a diverse group of materials and the like? Not all of these materials are exemplified by examples in the specification and therefore not all of these examples would be enabled even though listed.

Claims 1-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the following substances capable of changing dielectrophoretic properties: inorganic metal oxides, silica, alumina, metals, gold, titanium, iron, microorganisms, eukaryotic cells, polysaccharides macromolecular copolymer, styrene-methacrylate, agarose, cellulose, insoluble dextran, polystyrene

latex, styrene-butadiene copolymer, acrolein-ethylene glycol dimethacrylate copolymer, styrene-styrenesufonate latex, polyacrylamide, polyglycidyl methacrylate, polyacrolein-coated particles, crosslinked polyacrylonitrile, acrylic ester, acrylic ester copolymer, acrylonitrile-butadiene, vinyl chloride-acrylic ester and polyvinyl acetate-acrylate, nickel, erythrocyte, sugars, nucleic acids, proteins and lipids, does not reasonably provide enablement for and the like. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. No two methods used would be exactly the same for a separation because the molecules themselves have different properties which would affect a separation, let alone the combination of these materials with those in supra. Some of the combinations of materials in this paragraph and the one previously will not necessarily cause a change in the dielectrophoresis. How can one method cover another largely diverse group of materials and the like? Not all of these materials are exemplified by examples in the specification and therefore not all of these examples would be enabled even though listed.

Claims 1-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a substance binding to a specific molecule consisting of: antigen-antibody, sugar chain-lectin, an enzyme-inhibitor, protein-peptide chain, chromosome-nucleotide chain, nucleotide chain-nucleotide chain, does not reasonably provide enablement for bonding to another substance not yet listed. The specification does not enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Natural phenomena and naturally occurring compounds are not patentable, therefore the ability to put these in a solution for them to bind together would also not be patentable subject matter.

Claims 1-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the following labeling substances or testing methods: enzyme immunoassay (EIA), radioimmunoassay (RIA), fluoroimmunoassay (FIA), hybridization, alkaline phosphatase (ALP), p-galactosidase (p-Ga1), peroxidase (POD), microperoxidase, glucose oxidase (GOD), glucose-6-phosphate dehydrogenase (G6PDH), malate dehydrogenase and luciferase, Coomassie Brilliant Blue R250, methyl orange, radioisotopes, fluorescein, rhodamine, dansy, fluorescamine, coumarin, naphthylamine, europium (Eu), luciferin, isoluminol, luminal, bis-2,4,6-tritluorophenyl oxalate, phenol, naphthol, anthracene, 4-amino-2,2,6,6-tetramethylpiperidine-1-oxyl, 3-amino-2,2,5,5-tetramethylpyrroridine-1-oxyl, 2,6-di-t-butyl-α-(3,5-di-t-butyl-4-oxo-2,5-cyclohexadien-1-ylidenel-p-tolyloxyl, does not reasonably provide enablement for and the like. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. How could one produce a single instrument for each of these detection methods? One would choose the appropriate detection method based on the type of separation that was necessary and produce the best detection of the separated molecules. How can one method cover another largely

diverse group of materials and the like? Not all of these materials or testing methods are exemplified by examples in the specification and therefore not all of these examples would be enabled even though listed. Certain testing methods have already been patented and/or are in use, therefore it would be inappropriate to grant coverage for a known method of detection.

Claims 1-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for sample which is embodied by the following: body fluids, serum, plasma, cerebrospinal fluid, synovial fluid, lymph, excreta, urine and feces, does not reasonably provide enablement for "etc." and the like. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. Each of these fluids would require a different media such as a different buffer system and or concentration of materials depending on the separation to be done and the amount of separation required and detection required, therefore how can one method be adequate to cover each and every possibility to be used with an extremely complex system such as a bodily fluid and the like?

Claim 25 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for only dielectrophoretic forces, does not reasonably provide enablement for the combination of (a) dielectrophoretic forces and (b) forces selected from group consisting of electrophoretic forces and forces of a solution flow (forces by a mobile phase). The specification does not enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The examples given to justify the addition of claim 25 do not have sufficient support in the specification for the combination of (a) dielectrophoretic forces and (b) forces selected from group consisting of electrophoretic forces and forces of a solution flow (forces by a mobile phase).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4, 5, 6, 7, 14, 15, 16 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention and fails to point out what is included or excluded by the claim language. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors.

It is unclear in claim 1 whether molecules and specific molecule are the same or different substances. It is unclear in claim 1 what a kind of molecule would be. It is unclear whether the dielectrophoretic force in claim 1 is meant to be unspecified, positive dielectric force or negative dielectric force. It is unclear from claim 1 what the

upper limit of the electric field strength would be because the term "or higher" is indefinite.

Claim 1 recites the limitation "the dielectrophoretic force" in line 3. There is insufficient antecedent basis for this limitation in the claim. Claim 1 recites the limitation "the complex substance" in line 5. There is insufficient antecedent basis for this limitation in the claim. Claim 1 recites the limitation "specific molecule" in line 5. There is insufficient antecedent basis for this limitation in the claim. Claim 1 recites the limitation "the substance capable of changing dielectrophoretic properties of the specific molecule" in lines 5-6. There is insufficient antecedent basis for this limitation in the claim.

It is unclear in claim 2 whether the dielectrophoretic force is meant to be unspecified, positive dielectric force or negative dielectric force. It is unclear in claim 2 how one determines an amount on the basis of a measurement result because no method of measuring is claimed and no method of detection is given either.

Claim 9 recites the limitation "substance capable of changing dielectrophoretic properties of the specific molecule" in claim 8. There is insufficient antecedent basis for this limitation in claim 8.

The previous rejection with regard to claim 10 has been withdrawn based on applicant's amendment.

Claim 24 recites the limitation "having a size of 1 mm or less and the non uniform electric field is one having an electric field strength of 3.5 MV/m or less which is

caused by applying an applied frequency of 100 Hz to 10 Hz" in claim 1. There is insufficient antecedent basis for this limitation in the claim. Claim 1 does not give a size to the molecule that applicant wishes to separate. No frequency has been given in claim 1.

The previous rejections with regard to claims 19-23 have been withdrawn based on applicant's amendment.

Claims Analysis

Electric field strength is a variable calculated from voltage and distance between electrodes and therefore would be dependent upon the dielectrophoretic apparatus used and not on the method of separation, method of determining a component in a sample or method of detection employed. This property is based on a mathematical algorithm and may not be given patentable weight in these claims.

The claims are drawn to a substance capable of changing dielectrophoretic properties of a specific molecule. It is important to note that it has been held that the recitation that an element is "capable of" performing a function is not a positive limitation but only requires the ability to so perform. It does not constitute a limitation in any patentable sense. In re Hutchison, 69 USPQ 138.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-10, 15-17, 24-25 are rejected under 35 U.S.C. 102(e) as being anticipated by Parton, et al. (US 5993631).

Parton, et al. disclose a method of separating a first population of particles from a second population of particles where first population is bound to a ligand and a label which changes the properties of the first population of particles and the second is unbound affecting a separation between the first and second population in a dielectrophoretic field (col. 2, l. 46-58). The population of particles disclosed are mammalian cells, plant cells, yeast cells, chromosomes undergoing meiosis or mitosis, oocytes, other chromosomes, bacterial cells, viruses, DNA, RNA and proteins (aka "sample derived from a living body" - col. 3, l. 6-12). The ligands disclosed which bind to the particle can be an antibody, antigen, nucleic acid probe, nucleic acid analog, avidin or avidin like substance (col. 3, l. 31-37; Figures 8-12). Labels disclosed can be magnetic, fluorescent markers, chromophores, enzyme molecules or anything that will produce a detectible signal (col. 4, l. 36-60; Figures 9-12). It is disclosed that the separation between the microelectrodes is 30 μm to 80 μm which are 5 to 20 times larger than the size of the particles (col. 6, l. 52-57). At least one detection method is disclosed for detecting the separated particles (col. 7, l. 29-40; col. 8, l. 29-41; Figure 7). The dielectrophoretic force disclosed is based on the movement of the particle and

is related to the frequency of the rotating field from 10 to 10^{10} Hz (col. 11, l. 9-13; col. 12, l. 38 – col. 13, l. 23; Figures 14-16). The electrodes disclosed are capable of horizontal and vertical non uniform fields (Figures 1-6) and are disclosed as thin metal film electrodes o an insulating substrate, suitably gold electrodes printed on a glass slide (col. 6, l. 50-52).

Claims 1-10 are rejected under 35 U.S.C. 102(e) as being anticipated by Becker, et al. (US 6294063).

Becker, et al. teach an equivalence between movement of sample ("packets") by electrophoretic forces and dielectrophoretic forces (Figure 2; col. 3, l. 42-46; col. 7, l. 63 – col. 8, l. 5; col. 8, l. 31-35). Becker, et al. also teach a method of forming a complex substance to separate out a specific molecule from a mixture by applying a dielectrophoretic field then detection to give qualitative measurement of the separated specific molecule where the application deals with separation of proteins, nucleic acids and cells (Figures 1, 9B, 12; col. 2, l. 59-63; col. 3, l. 17-23; col. 4, l. 6-10; co. 5, l. 66 – col. 7, l. 4; col. 14, l. 46 – col. 15, l. 7; col. 28, l. 28 – col. 30, l. 44).

Response to Arguments

Applicant's arguments filed 11/15/2005 have been fully considered but they are not fully persuasive.

1. Previous claim objections have been withdrawn.

2. 112 rejections have been indicated as withdrawn or have been maintained as stated above. New 112 rejections have been given to request clarification of applicant's special way of defining the terminology enclosed in quotation marks.

3. In response to applicant's argument that the Parton, et al. (US 5993631) reference fails to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., eth method of the present claims does not use TWFM) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Since the Examiner is not privileged to the specific device other than what was disclosed by applicant and cannot assume the exact dimensions, an accurate calculation of the field strength of Parton, et al. cannot be made but must be assumed to be present as an inherent property until proven otherwise. Applicant has not provided any showing of unexpected results, what specifically is unexpected about said results or how the electric field strength of 500 kV/m or more would provide said unexpected results. The previous rejection has been maintained.

4. Becker, et al. specifically teach an inhomogeneous dielectrophoretic field (AC or DC) may be applied (see column 8, lines 31-32) and further states that "any signal parameter may be varied and any electrode selection may be controlled so that appropriate electric fields may be established at particular locations upon reaction surface ... Alternating Current or Direct Current signals may be utilized." (col. 16, l. 4-7).

Therefore apparatus of Becker, et al. would be able to provide an electric field in the strength of 500 kV/m or higher. Applicant has not sufficiently distinguished the claim language over that of Becker, et al., therefore the previous rejection has been maintained.

Relevant Prior Art

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

US 5344535 discloses dielectric characterization of micro-organisms and other particles where the dielectrophoretic apparatus comprises gold or aluminum electrodes, application of a spatially non-uniform alternating electric field, having a frequency between 10 Hz to 10 MHz, and inherent electric field strength which can be calculated using a distance between electrodes of 0.06 mm and 5-30V. The apparatus is used to separate out staphylococcus areus, pseudomonas fluorens, E coli and B cereus and detection is made through a light detector.

Conclusion

Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennine M. Brown whose telephone number is (571) 272-1364. The examiner can normally be reached on M-R 9:30 AM - 7:30 PM; Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jerry Lorengo can be reached on (571) 272-1233. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

jmb